

Spring 1995

## Focal Spot, Spring 1995

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SPRING, 1995

VOLUME 26, NUMBER 1

# FOCAL SPOT

MALLINCKRODT INSTITUTE OF RADIOLOGY

DISCOVER  
TREAT REFLECTIONS  
HEAL





The official centennial poster by artist Greg Harlin was commissioned by Radiology Centennial Incorporated (RCI).



As Hartman Orator and the 16th Malcolm Jones Lecturer, MIR Director Ronald Evens spoke on "The History of Postgraduate Education in Radiology" at the April meeting of the American Association of Academic Chief Residents in Radiology (A<sup>3</sup>CR<sup>2</sup>). In recognition of 100 years of achievements in the radiation sciences, throughout the year radiology leaders will present Hartman Orations at society and educational meetings worldwide. The orations are named in honor of the late Dr. Glen Hartman, a professor of radiology at the Mayo Clinic, who spearheaded the Radiology Centennial.

After the lecture Evens gathered with MIR diagnostic radiology residents (left to right) Farrel Van Wagenen, 1995-1996 cochief; Cynthia Rigby, '94-'95 chief; Eric Weidman, '95-'96 chief; and Sean Muldowney, '94-'95 cochief.



## REFLECTIONS

**W**ilhelm Conrad Roentgen would be amazed at the advances made in radiology since **1895** when he produced that first picture of the bones in his wife's hand. And Doctors Warren Cole, Glover Copher, Evarts Graham, and Sherwood Moore of Washington University would be proud that their first gallbladder visualization was the impetus for building what has become one of the world's premier radiological institutions — **MALLINCKRODT INSTITUTE.**



In the 64 years since the Institute began operation, MIR scientists and clinicians have provided essential information for the diagnosis and treatment of diseases. From the development of roentgen kymography and positron emission tomography to the first medical application of isotopes, from identifying clinical applications for three-dimensional imaging to functional mapping of the brain — all of this groundbreaking research, and more, has come out of Mallinckrodt Institute of Radiology.

At MIR, scientists and clinicians are committed to providing the highest quality health care possible. Through their search to **DISCOVER** newer and better methods for **TREATING** and **HEALING** diseases, the quality of life for thousands of patients has already improved. The following pages provide updates on some of that research and the changes affecting the Institute.







**T**he affiliation between Washington University School of Medicine (WUMS) and Barnes Hospital began over 80 years ago. Back in October of 1911, a contract was drawn up with the provisions that the yet-to-be-built hospital would not only be staffed by WUMS faculty but would serve as the home base for the School's research and medical education.

Since it first opened in 1931, the Institute has provided diagnostic radiology services for Barnes and, later, for Children's Hospital of St. Louis. Within the last five years, MIR's responsibility for diagnostic services dramatically increased. Robert Levitt, MD, director of radiology at Barnes West County Hospital, coordinated the **EXPANSION** of diagnostic services at this satellite hospital and, in the past academic year, produced a volume increase of more than 25 percent over previous years. Since early 1994, Scott Mirowitz, MD, radiologist-in-chief, has guided a renovation of the diagnostic radiology facilities at Jewish Hospital. In July of 1994, William Dawson, MD, was appointed radiologist-in-chief of Mallinckrodt Institute's Department of Radiology at Barnes St. Peters Hospital. Plans are underway to include additional services and to enlarge the diagnostic clinical areas.

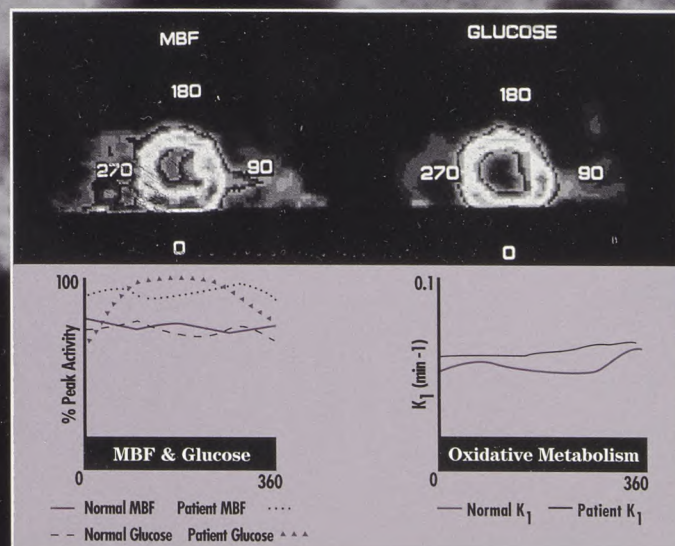
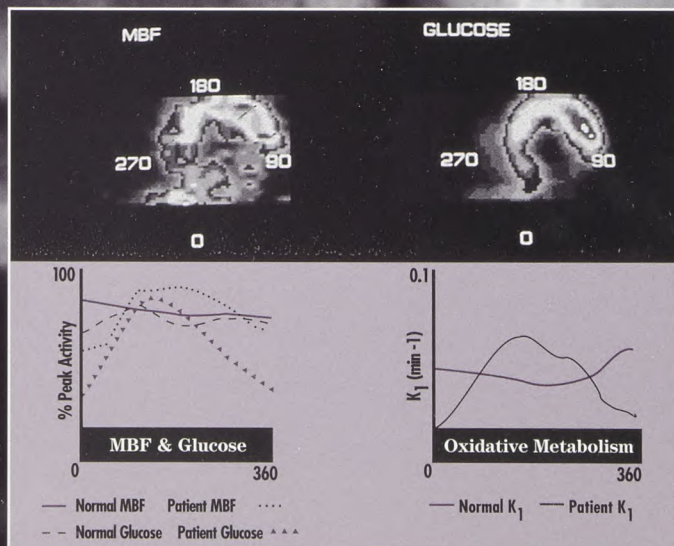
In 1948, MIR's Radiation Oncology Center first offered high-energy radiation therapy to Barnes Hospital patients who were diagnosed with cancer, and the program was expanded in late 1983 to include Jewish Hospital. Subsequent years were marked by refinements in treatment techniques and a steady increase in treatment programs, with a tremendous growth spurt in 1994: a three-dimensional planning and quality assurance facility; a brachytherapy lab where physicists develop better methods for targeting cancers with sealed, radioactive isotopes; and, a simultaneous hyperthermia and external beam program at Jewish Hospital for treating small and large superficial tumors.

The Institute's soon-to-be 30-year-old Division of Nuclear Medicine provides diagnostic nuclear medicine procedures at Barnes, Jewish, and Children's hospitals and consultation services at Barnes West County and Barnes St. Peters. During the 1993-1994 academic year, MIR introduced the St. Louis region's **FIRST NUCLEAR IMAGING** with the gamma-emitting compound Octreoscan<sup>®</sup>. Collaborating with clinicians in the WUMS Cardiovascular Division, nuclear medicine physicians have laid the groundwork for an integrated cardiac stress imaging service.

By the end of 1994, the Institute was providing professional services for five hospitals, and another superlative — the largest academic radiology department in the United States — was added to MIR's list of recognitions. While bigger is not synonymous with better, the Institute proved that additional clinical responsibilities has not altered our ultimate goal: providing patients and their physicians with the highest quality radiology services. In a recent Barnes Hospital Physician Satisfaction Survey, referring physicians rated their level of satisfaction with medical services, and MIR's diagnostic radiology and radiation oncology clinical areas each **RECEIVED TOP RATINGS**, an impressive 94 percent "very satisfied." **MIR**



# 180





**L**ife is a gamble, but perhaps no one is more aware of that gamble than the seven million patients in the United States who have

## CORONARY ARTERY DISEASE.

With this disease, fatty deposits line the arteries supplying blood to the heart muscle. When those deposits harden and obstruct blood flow in the arteries, odds are high that the patient will experience pronounced chest pain or a heart attack. The odds are even greater that part of the heart muscle will die. Until now there was no diagnostic procedure that could accurately predict if the myocardium was damaged but still alive, or if patients would benefit from angioplasty or surgery.

At Mallinckrodt Institute, **DR. ROBERT GROPLER** of the Division of Nuclear Medicine has successfully used positron emission tomography (PET) to measure the correlations among blood flow, glucose utilization, and oxygen consumption in the heart. Blood flow may be decreased but if oxygen and glucose are being used, then the heart muscle is metabolically active. And viable muscle means the patient is a good candidate for balloon angioplasty or bypass surgery.

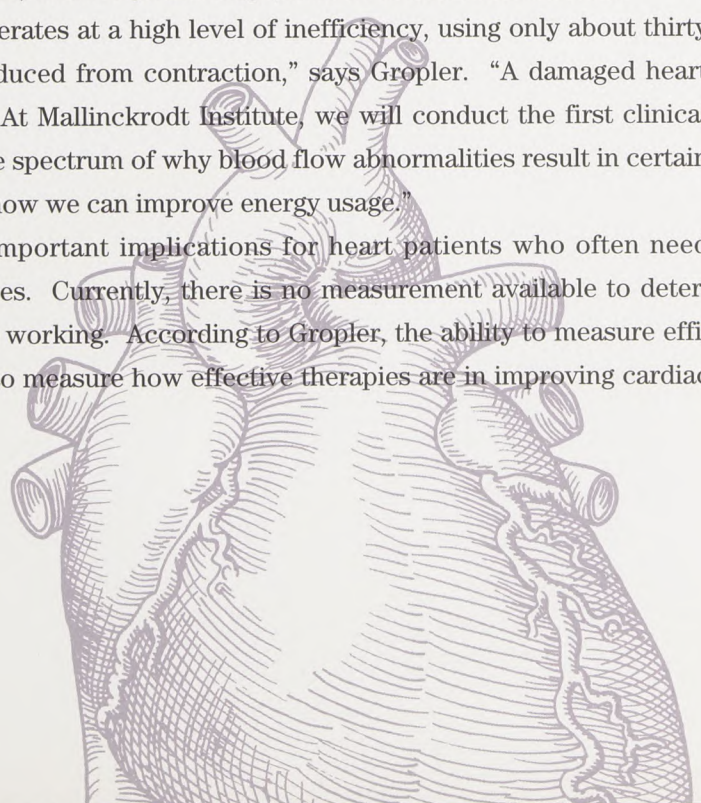
In a three-year study of more than 100 patients, an oxygen usage measurement with the radiolabeled compound  $^{11}\text{C}$ -acetate proved to be the most accurate PET measurement available to determine cardiac tissue viability. Study results are impressive. Eighty-five percent of the patients diagnosed with viable heart muscle have improved muscle function as a result of angioplasty or surgery, and they were either taken off medication or the dosage was reduced. If the myocardium was determined to be non-viable, the PET diagnosis correctly predicted (90 percent) that metabolic function would not return.

Now a routinely offered clinical test at the Institute, the 45-minute, **CARDIAC PET**-with-acetate procedure is more time efficient than other diagnostic exams. Standard imaging with  $^{18}\text{F}$ -fluorodeoxyglucose (measures how much sugar the heart metabolizes) takes nearly three hours to complete; thallium stress imaging, up to four hours.

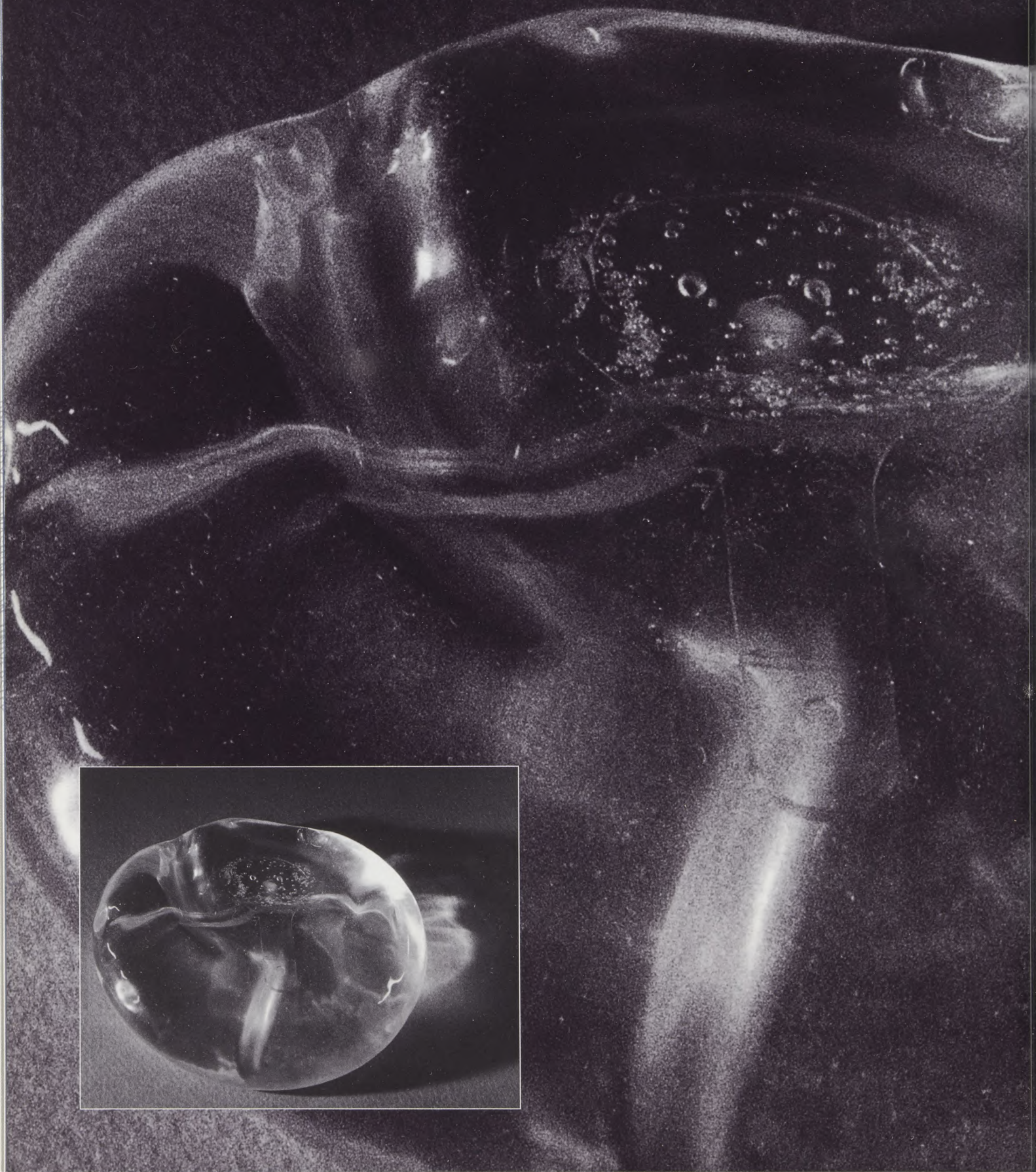
While continuing to track patient outcomes from the acetate study, Gropler will use PET to explore another facet of cardiac metabolism — measuring the energy efficiency of heart muscle. As principal investigator of a five-year, National Institutes of Health grant, Gropler, in collaboration with Washington University cardiologists, will study a group of 200 patients, 45 to 70 years of age, who have had a heart attack.

"A normal heart operates at a high level of inefficiency, using only about thirty percent of the energy produced from contraction," says Gropler. "A damaged heart uses five percent or less. At Mallinckrodt Institute, we will conduct the first clinical investigation into the entire spectrum of why blood flow abnormalities result in certain myocardial functions and how we can improve energy usage."

The research has important implications for heart patients who often need aggressive medical therapies. Currently, there is no measurement available to determine if these therapies are working. According to Gropler, the ability to measure efficiency will provide a way to measure how effective therapies are in improving cardiac function. **MIR**









*It has been 30 years since augmentation mammoplasty was first available in the United States. And it has been four years since the Food and Drug Administration (FDA) banned the silicone gel prosthesis used for breast enlargement. The ban came on the heels of thousands of lawsuits claiming that some women's illnesses were caused by the leakage of silicone gel from their implants.*

But long before the national controversy over **IMPLANTS** hit the news, radiologists at Mallinckrodt Institute were concerned about another problem stemming from augmentation mammoplasty: 22 to 83 percent of breast tissue was blocked on mammograms because of the implant's opacity to X rays, and that opacity could cause early-stage breast cancer to go undetected. **DRS. LOUIS GILULA, BARBARA MONSEES**, and former colleague Judy Destouet were joined in their search for a new, radiolucent breast implant filler by Leroy Young, a Washington University plastic surgeon, and **JOHN EICHLING, PhD**, an MIR medical physicist.

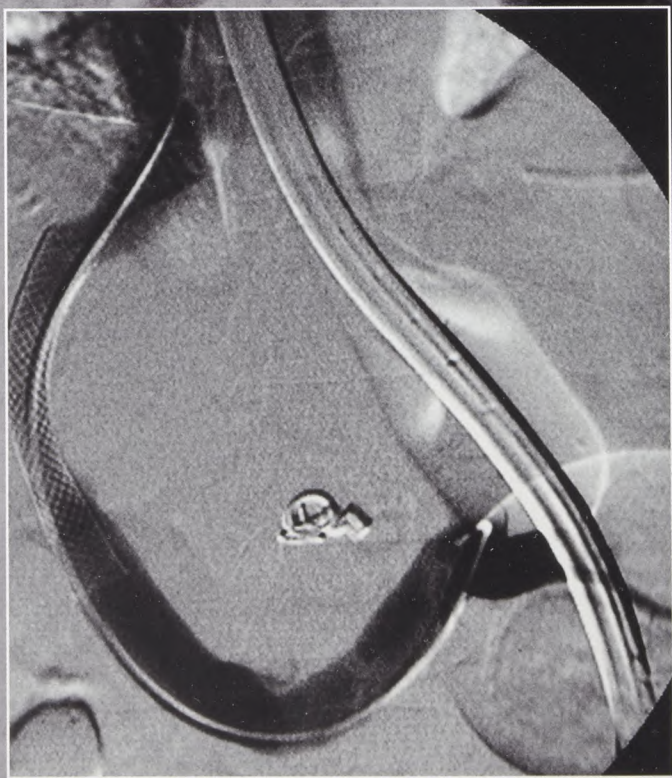
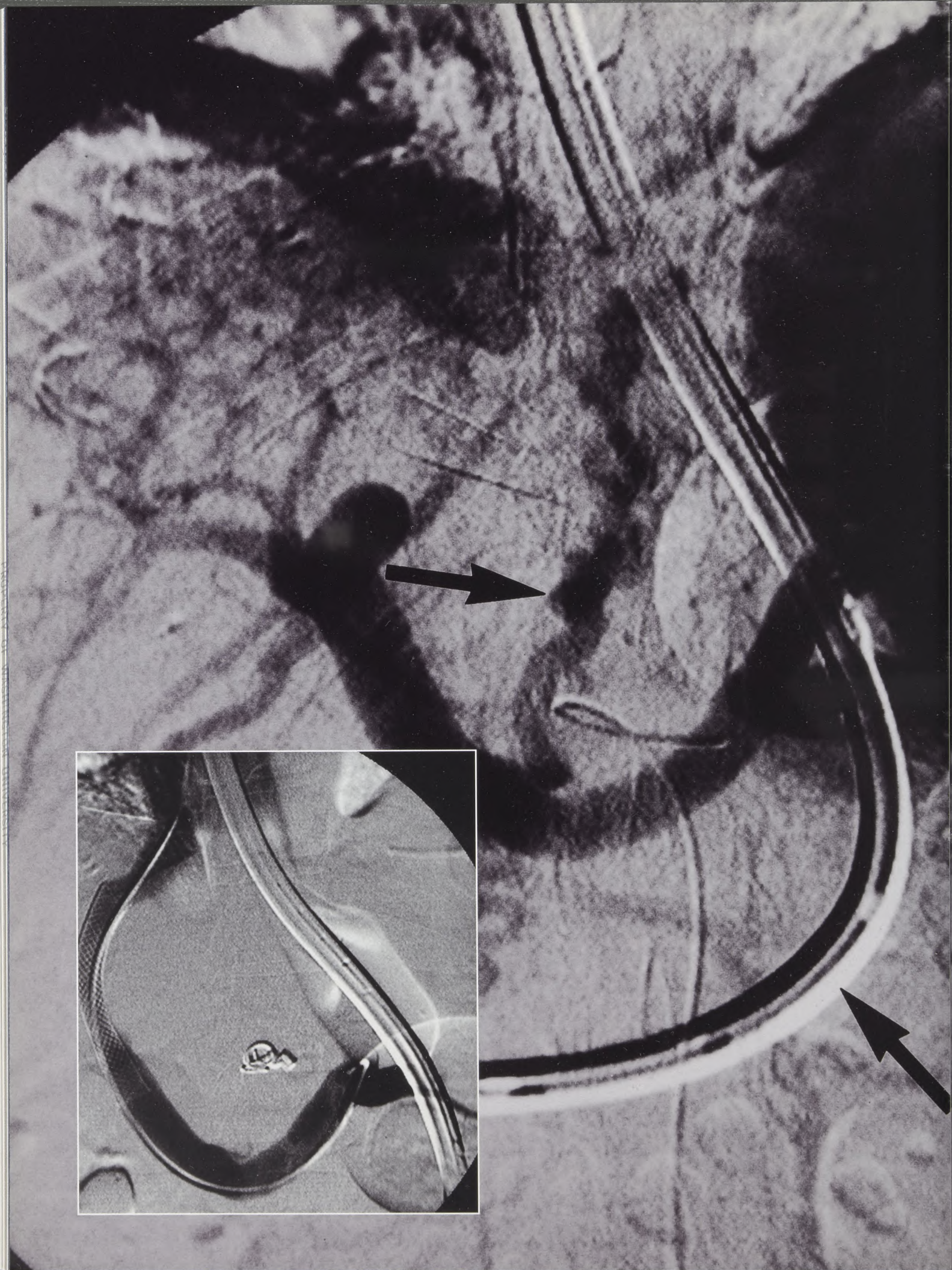
The first breakthrough came with Eichling's demonstration that triglyceride, a naturally occurring fat that can be metabolized by the body, was similar in opacity to normal breast tissue. After subsequent testing of experimental implants filled with triglycerides (such as peanut and sunflower oils) provided positive results, the researchers were awarded a patent for a radiolucent breast implant filler.

In August of 1994, the FDA approved a five-site, national study to pre-market test **TRILUCENT<sup>®</sup>**, an implant filled with a natural fat from soybean oil. Trilucent, manufactured by LipoMatrix Inc. of Palo Alto, California, in conjunction with the Washington University-held patent, also contains a small computer chip (called a transponder) that is individually coded and stores medical information about the patient and the implant. The information, which can be noninvasively retrieved with an electronic scanning device, will be entered into an international registry database for future follow-up.

Women participating in the study all have augmentation implants that must be removed because of leakage or other complications not related to systemic medical problems. There are 10 patients at each of the five clinical trials — **WASHINGTON UNIVERSITY**; Johns Hopkins University; The Breast Center in Van Nuys, California; the University of Florida in Gainesville; and Stanford University.

Study participants will receive medical follow-up for at least one year following implantation. In addition to assessing the implant's radiolucency, researchers will assess capsular scarring tendencies, anatomic benefit, and changes in the patient's quality of life. Drs. Monsees and Young are principal investigators of the Washington University study, where the first of the 50 patients received the Trilucent implant in December. **MIR**







*In the summer of 1992, there were approximately 500 critically ill patients worldwide who owed their lives to a piece of metal and an interventional radiology procedure called **TIPS** — transjugular intrahepatic portosystemic shunting.*

**A**ll of the patients had developed life-threatening, esophageal or gastric bleeding problems caused by chronic, progressive liver disease. When the blood flow between the portal vein (transports blood from the bowel and spleen to the liver) and an hepatic vein (receives blood from the liver) is blocked, pressure builds up in the portal vein and causes bleeding. If the bleeding is not controlled, the patient can die.

There are methods other than TIPS that can treat the bleeding: endoscopic sclerotherapy or surgical portosystemic shunts. But both carry risks. Injecting solutions into the esophagus to cause clotting carries a high incidence of recurrent bleeding and up to a 20 percent complication rate. And although a surgical shunt will stop the hemorrhaging, the major surgery involved often results in high mortality rates, plus additional surgery is required to remove the shunt during liver transplantation.

At the Institute, **DR. MICHAEL DARCY** has led an interventional radiology team through 125 TIPS procedures to date. In TIPS, an expandable, metallic stent is guided through a sheath placed in the patient's jugular vein and into the liver. This shunt forms a **NEW PATH FOR THE BLOOD FLOW** and removes the pressure from the portal vein. The MIR team has perfected the method of finding the portal vein by modifying the angiographic techniques and using an innovative needle system.

Hailed as a godsend by both patients and physicians, TIPS involves no surgery. The procedure does require a local anesthetic and IV sedatives but is more easily tolerated by a critically ill patient than either of the alternatives. Downtime for the patient is usually one or two days in the hospital. There are no complications if the patient subsequently undergoes liver transplantation because the shunt is completely within the liver and is removed with the liver during the transplant.

TIPS procedures were first done in the 1960s, using balloon dilation to open a tract in the liver between the portal and hepatic veins. Results were not often good because the pathway would quickly close down. The solution came in 1989 in the form of a metal, balloon-expandable stent to permanently create a blood flow path.

As MIR's principal investigator in a Federal Drug Administration-approved, multi-center trial, Darcy is evaluating the efficacy of TIPS with a new self-expanding, flexible stent. The three-year-old trial is nearing completion, and researchers are reporting good results. The majority of the patients in the study have greatly benefitted from TIPS. **MIR**







**F**rom the shopping mall to the operating room is an unlikely progression by any stretch of the imagination. But technology developed in 1983 to produce portrait sculptures sold in U.S. shopping malls is now used successfully by plastic surgeons in the pre- and postoperative evaluation of their patients.

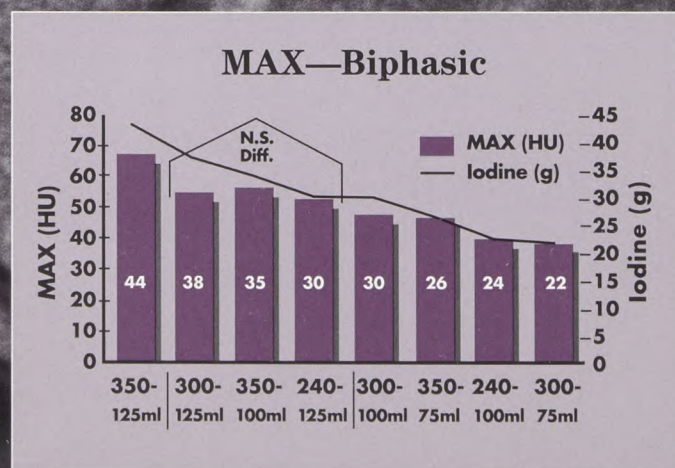
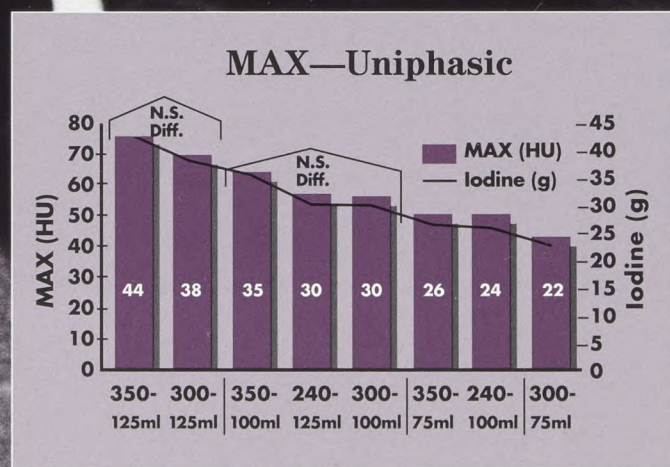
About five years ago, **MICHAEL VANNIER, MD**, director of the Institute's image processing lab, was contacted by researchers from a small St. Louis company called Cencit, Inc. to help create a new market for their scanner. Vannier, a pioneer in **3-D IMAGING** with expertise in congenital facial deformities, and a team of MIR engineers designed software and techniques to convert an existing sensing device into a medical facial-surface scanner.

The resulting three-dimensional surface digitizer produces a 360-degree examination of the head in less than one second. The free-standing, geodesic-shaped structure houses six cameras and six strobe-light projectors, which work on a "patterned light" concept using ordinary white light. A zigzag pattern or grid, projected onto the patient's face, produces 144 images. The images are processed into 3-D data for comparison with changes measured one day after surgery and again after two weeks.

In 1991, Vannier and Leroy Young, MD, Washington University plastic and reconstructive surgeon, conducted a study of the new imaging system. The first patient was a 41-year-old female who underwent facial plastic surgery: forehead lift, eyelid surgery, chin implant, and facelift. Study results prove the system's **ACCURACY IN MEASURING CHANGES** resulting from surgery and in identifying and quantifying postoperative facial edema. The system's ability to distinguish changes due to surgery from those due to edema aids surgeons in prescribing steroidal therapy for patients. By modifying the data, surgeons can show their patients a computerized preview of the postoperative results and can calculate the correct size, shape, and volume of an implant.

Encouraged by the success of the facial scanner, Vannier and the research team are exploring suitable **APPLICATIONS FOR WHOLE-BODY SCANNING**, such as orthotic and prosthetic design, breast reconstruction surgery, reduction and augmentation mammoplasty, scoliosis assessment, and radiation treatment planning. Vannier, a consultant to the Advisory Group for Aerospace Research and Development (NATO's oldest scientific and technical arm), says his motivation for whole-body scanning research comes from the group's quest for a multinational standard-sizing system. Vannier hopes to use 3-D surface imaging techniques, coupled with the expertise of Michael Miller, a Washington University electrical engineering professor recognized for his mathematical evaluations of shape and size variations, to produce a universal measurement system for medical, governmental, and industrial applications. **MIR**







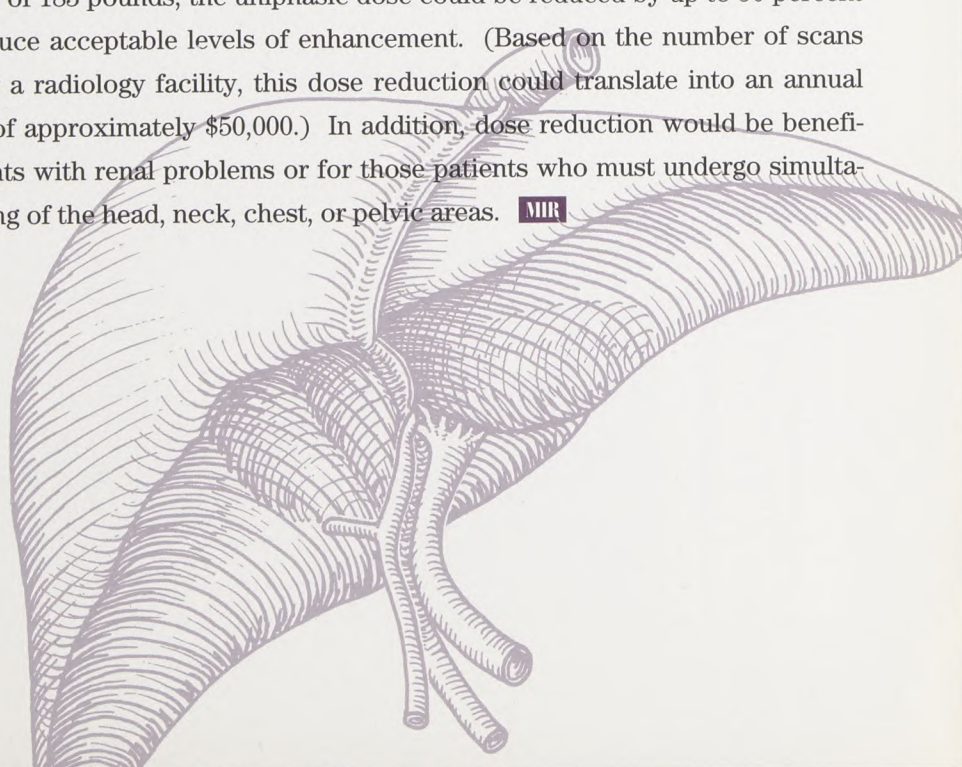
**S**piral computed tomography (CT): a technology that promises to be less invasive, less costly, and as equally effective as other procedures in diagnosing diseases. Across the country, researchers are conducting large-scale studies to determine whether spiral CT can make good on those promises.

Helical or spiral CT operates on a slip-ring technology; the X-ray tube and detector rotate continuously in a **360-DEGREE SPIRAL MOTION** around the patient. Since the patient takes only a single breath-hold (as compared to one, five-second breath-hold for each of the 24 slices on conventional CT), the risk of respiratory misregistration and motion artifacts on the scan is virtually eliminated. Total scanning time ranges from a few seconds up to one-half minute, as compared to two to three minutes with conventional CT, and the imaging quality of the two technologies is comparable.

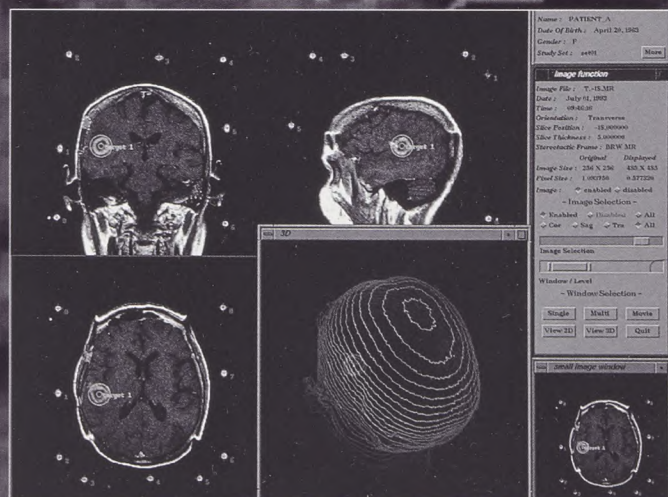
But in an era where health care dollars are under scrutiny, the cost-effectiveness of spiral CT is being questioned. Proponents claim that **SPIRAL CT** can produce high quality scans while using less contrast media. Opponents of this theory are concerned that to be competitive financially, the dose of contrast media would be reduced to levels that affect the quality of the scan and, ultimately, the diagnosis.

At Mallinckrodt Institute, **JAMES BRINK, MD**, is principal investigator of a chest and abdominal study to determine the optimal dosage and delivery method of contrast media used with spiral CT. The Institute's 800-patient study is funded by the Society of Computed Body Tomography and Magnetic Resonance and by Nycomed Incorporated (formerly Sanofi Winthrop). The chest portion of the study is nearly complete, with 75 of the 300 patients remaining to be scanned using low-dose protocols. The completed, abdominal portion of the study involved 487 patients, randomly placed into 17 groups. Eight groups received contrast injected at a constant, single rate (called uniphasic); 9 groups received a higher injection rate at the beginning of the scan, a slower rate near the end (biphasic).

The abdominal scans showed that uniphasic injection universally provided better results than did biphasic injection. For patients weighing less than the groups' mean average of 183 pounds, the uniphasic dose could be reduced by up to 50 percent and still produce acceptable levels of enhancement. (Based on the number of scans performed by a radiology facility, this dose reduction could translate into an annual cost savings of approximately \$50,000.) In addition, dose reduction would be beneficial for patients with renal problems or for those patients who must undergo simultaneous scanning of the head, neck, chest, or pelvic areas. **MIR**







**MIR 3D RTP System**  
 Name: Patient A ID: A  
 MD: field 2 Site: field 1  
 planid: Final As treated  
 Treatment position: Head to Gantry

isocurve List (cGy)	color	surface rendering
-2100.00	-D MAGENTA	-W
-1800.00	-RED	-W
-1400.00	-GREEN	-W
-1000.00	-BLUE	-W
-800.00	-YELLOW	-W
-500.00	-CYAN	-W
-300.00	-MAGENTA	-W
-200.00	-ORANGE	-W
-100.00	-PURPLE	-W
	-D RED	-W
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	-D BLUE	-W
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	-D CYAN	-W
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maximum dose 2349.6  
 DONE



**A**n interactive software package developed in Mallinckrodt Institute's radiation physics labs is adding another dimension to the radiotherapy treatment of brain tumors. During the past two years, as principal investigator for a contract from Kanematsu Medical Systems of Tokyo, **ROBERT DRZYMALA, PhD**, has developed and fine-tuned a portable software package for visualizing anatomy and radiation doses in multiple two-dimensional and three-dimensional views. The technology will be tested within the year in clinical trials at Jewish Hospital.

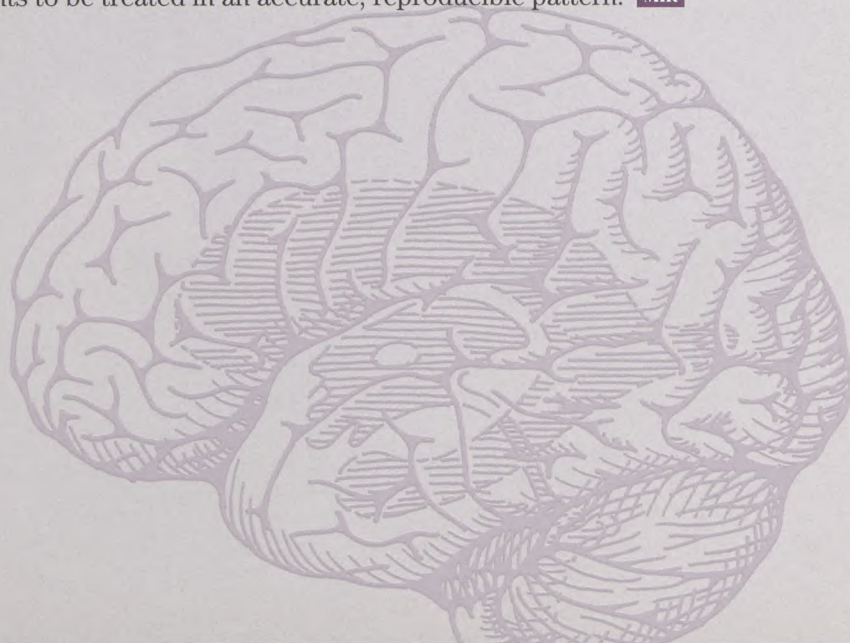
The software package can run on high-end workstations that support X-windows. Used in tandem with imaging equipment such as computed tomography, positron emission tomography, magnetic resonance, and digital angiography, the software is a boon to radiotherapy treatment planning — both for the clinician and the patient.

While the current system for simulating and planning **STEREOTACTIC RADIOTHERAPY** is effective, dose calculations are formatted two-dimensionally, one angle at a time. Coupled with a slow workstation, the treatment planning routine is long and laborious. The new software dovetails with the Institute's 3-D treatment planning system, with a special modification for the brain. This modification provides input for locating the center of radiation beams and for calculating radiation doses.

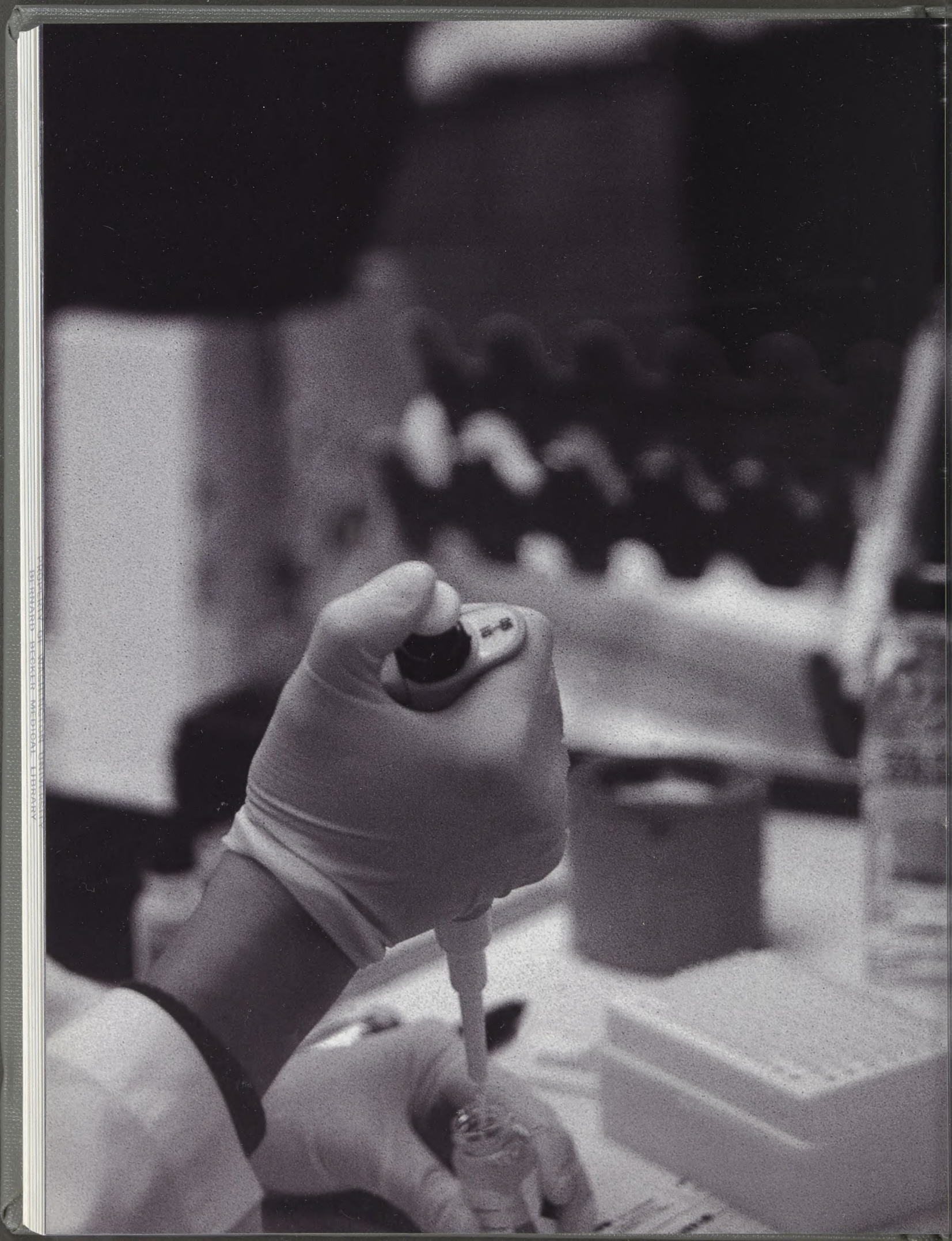
During the scanning procedure, the patient's head is immobilized with a stereotactic frame that appears as dots on the scans. This **DOT PATTERN** indicates a definitive coordinate system that targets the radiation beam within one millimeter of the tumor. The high-speed workstation immediately shows multiple 2-D and 3-D views of the target area with 3-D dose distributions. Since both the planning and treatment usually can be accomplished in one day, the method is cost-effective, time efficient, and less stressful to the patient.

The system also can aid neurosurgeons in planning brain tissue biopsies; implanting devices used in functional disorders, such as epilepsy, to chemically or physiologically manipulate brain tissue; and in treating arterial venous malformations and other vascular abnormalities.

Drzymala and coinvestigators **JOSEPH SIMPSON, MD, PhD**, a radiation oncologist, and Keith Rich, MD, a neurosurgeon, plan to further develop the software to include an expanded marking or coordinate system for analyzing anatomy orientations. Then, the cumbersome stereotactic frame now used can be replaced with a simpler version. A 3-D digitizer will locate the markers established during the initial treatment planning and transfer the coordinates to the radiotherapy equipment, allowing patients to be treated in an accurate, reproducible pattern. **NMR**









*If you say that John or Mary has a certain glow about them, you are usually referring to their supposed good health. When researchers in MIR's Radiation Sciences laboratories talk about a certain glow, they are probably discussing studies using positron emission tomography (PET) and the glow emitted by a tiny, metal-bearing peptide — studies that promise to reclaim good health for cancer patients.*

For many years, researchers have known that cancers grow more rapidly if they carry receptors for specific hormones naturally produced within the body. If scientists can use radiolabeled, manmade hormones (called octreotide) that will attach to the cancer cells, then the cell growth can be slowed or stopped. And if researchers can produce on-site a less expensive alternative to the commercially produced octreotides, then research dollars can be better applied to the fight against cancer.

Receptors for one of these natural hormones, **SOMATOSTATIN**, are carried by cancerous cells in the neuroendocrine system as well as tumors of the prostate, breast, and lung. In the summer of 1994, as principal investigator, **CAROLYN ANDERSON, PhD**, received a five-year, National Institutes of Health grant to evaluate whether or not radiolabeled octreotide would bind to cancer cells containing somatostatin receptors.

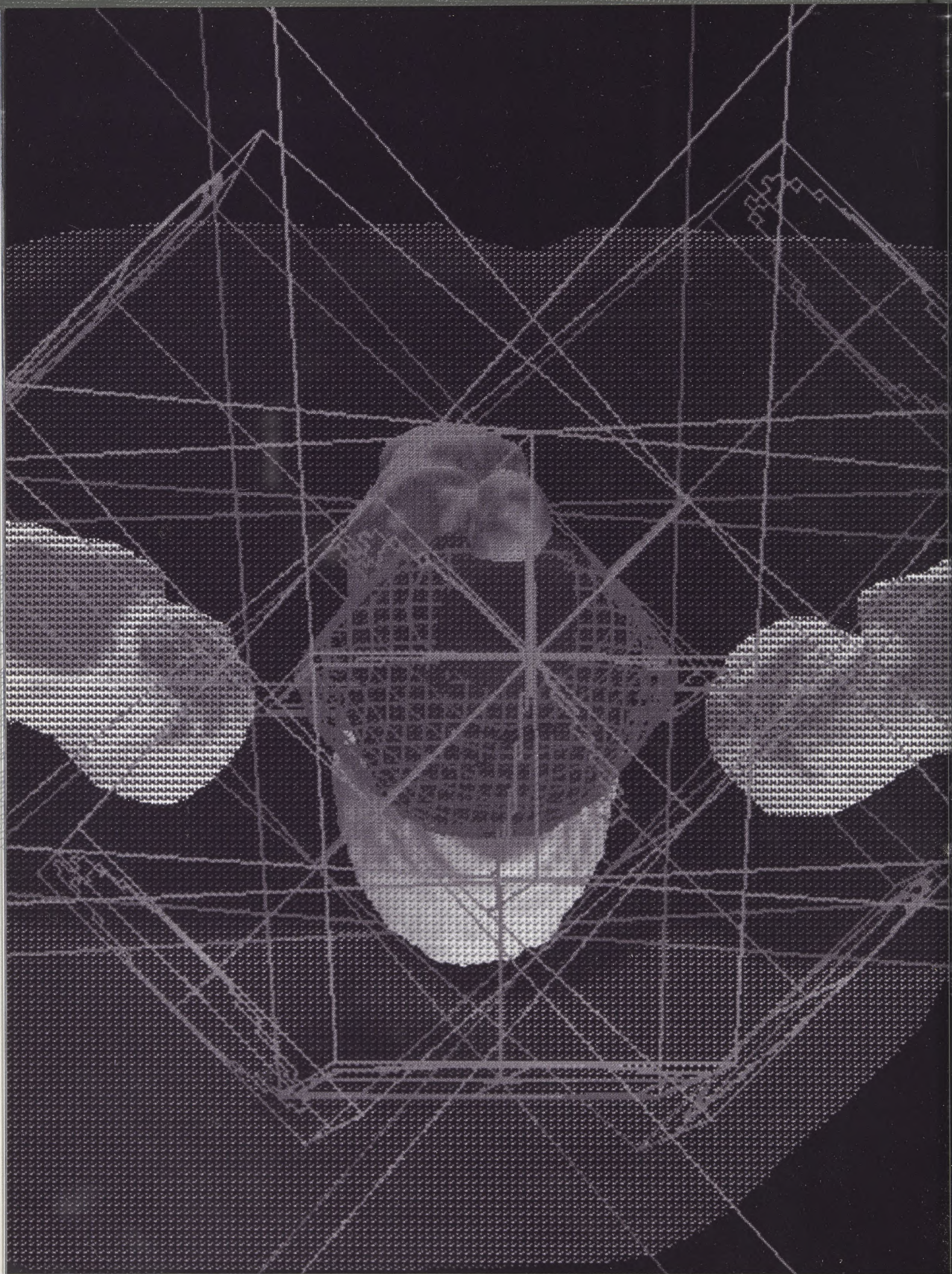
Anderson and her research team have now developed two octreotide analogs for radiolabeling with copper-64 and have evaluated the analogs in cells and in animal models. By labeling octreotide with copper-64, a positron-emitting metal, the scientists plan to set a trap: If the cells carrying somatostatin receptors bind with octreotide, the sites will glow when scanned with PET. Successful results would give oncologists a powerful tool in the diagnosis or treatment of certain cancers.

Details of the team's octreotide syntheses were published in the *Journal of Medicinal Chemistry*. The evaluation of the radiolabeled analogs is scheduled to appear in the *Journal of Nuclear Medicine*.

The next phase of Anderson's research is a **COLLABORATIVE CLINICAL STUDY** of small cell lung cancer (SCLC) tumors. In previous clinical studies using a gamma-emitting compound, large concentrations of somatostatin receptors were found in SCLC tumors. Anderson will work with **FARROKH DEHDASHTI, MD**, principal investigator of the clinical protocol, to evaluate somatostatin-receptor levels in SCLC tumors imaged by positron emission tomography and a copper-64 labeled octreotide analog.

"Our goal is to define the potential role of PET utilizing copper-64 labeled octreotide as a noninvasive imaging technique in the management of SCLC," says Anderson. "If successful, we hope to expand the use of positron-emitting octreotide analogs and PET to include the management of other somatostatin-receptor positive tumors." **MIR**







*A nine-year-old "newcomer" — three-dimensional radiation treatment planning and conformal therapy — is rapidly joining the ranks of traditional radiation oncology armamentarium. Buoyed by the increasing numbers of radiation oncology centers worldwide that are recognizing the value of 3-D treatment, MIR's **JAMES PURDY, PhD**, one of the technology's pioneers, proposes that "radiation oncology will be an integrated, image-based medicine within five years."*

Three-dimensional treatment planning began in 1986 as a call to action by the National Cancer Institute: Create a program for delivering high-energy radiation safely and more precisely to the tumor site while sparing surrounding healthy tissue. Including MIR, six institutions nationwide were involved in developing the groundbreaking technology. Purdy, chief of radiation physics, was principal investigator for two research contracts that led to the development of a 3-D dose planning system. The technology was later approved by the Food and Drug Administration and is now sold commercially.

The St. Louis area's first **3-D TREATMENT PLANNING** center opened at Mallinckrodt Institute in July of 1992. The center, housed in the radiation physics area on the sixth floor of Barnard Hospital, was equipped with an existing computed tomography (CT) scanner fitted with a special laser marking system and connected to a 3-D treatment planning computer.

At MIR, treatment for 50 percent of patients requiring advanced planning is prescribed through the 3-D program; the most prevalent application is for lung and **PROSTATE** cancer. During the last year, workstations interfaced with 3-D planning systems were installed in the radiation oncology clinical areas at Barnes and Jewish hospitals and in the radiation physics preplanning room. At the heart of these systems is a new, commercially produced **CT SIMULATOR** with an integrated laser marking system. The addition of multileaf collimation — devices installed on two linear accelerators and connected over the computer network to the planning system — provides conformal therapy for an average of 40 patients per month.

A Quality Assurance Center, established in late 1994, is the clearinghouse for patient data submitted by nine facilities participating in a national dose escalation protocol for localized carcinoma of the prostate. After each case is reviewed by a three-man assessment team (Purdy; Dr. Jeff Michalski, a radiation oncologist; and William Harms, a radiation physicist), results will be stored in a Washington University-developed database that will serve as a **NATIONAL RESOURCE** for the analysis of similar dose escalation programs.

A second national protocol for 3-D treatment planning of lung cancer is currently under development by the Radiation Therapy Oncology Group. Approval is scheduled for the fall of 1995; Bahman Emami, MD, clinical director of MIR's 3-D program; Mary Graham, MD; and Purdy will chair the MIR/Barnes Hospital studies. **MIR**

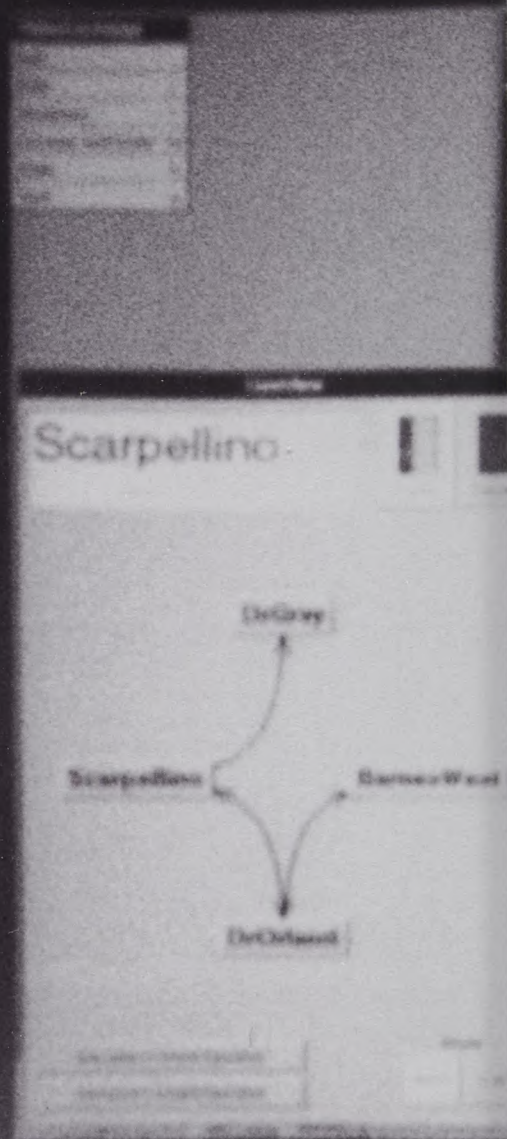




P R O J E C T

**SPECTRUM**

ADVANCED CLINICAL INFORMATION SYSTEMS





*A technology-driven collaboration among industry and medical giants promises to make health care more convenient, more efficient, and more cost-effective. With that promise comes the realization of MIR's ten-year-old dream of a high-speed, fiber optic communications system to transmit voice, data, video, and high-resolution images.*

In the mid-1980s, **GILBERT JOST, MD**, chief of Diagnostic Radiology, and **JAMES BLAINE, DSc**, director of the Electronic Radiology Laboratory (ERL), worked on the "Fast Packet Project" with Jonathan Turner, PhD, and Jerome Cox, ScD, of the University's Department of Computer Science. With support from Southwestern Bell and several other corporate sponsors, the researchers' goal was to develop a high-speed ATM communications system to support the electronic storage, transmission, and display of medical images. That collaboration, in part, laid the groundwork for "**PROJECT SPECTRUM**," a three-year program that will provide uniform integration of patient information from all BJC hospitals, electronic availability of patient records for BJC-affiliated physicians, and accessibility of data and images from all BJC hospitals.

BJC Health System, Washington University School of Medicine and Mallinckrodt Institute, IBM, Eastman Kodak, and Southwestern Bell comprise Project Spectrum's initial partnership; additional industrial members of the consortium are anticipated. The project's first phase began in mid-1994 with the development of prototype systems for both clinical information management and electronic image management. High-speed telecommunications links (155 megabits per second) are in place at all hospitals currently served by Mallinckrodt Institute. A comprehensive clinical data repository soon will include patient information gleaned from thousands of medical records stored at 15 BJC hospitals and affiliates.

A three-member executive committee steers Project Spectrum — Jost; David Weiss, director of BJC's management information systems; and Dr. Mark Frisse, associate dean for the School of Medicine's academic information management. In his capacity on the executive committee, Jost is responsible for coordinating the overall activities of the project and is specifically responsible for issues related to medical images.

Blaine and Dr. Michael Kahn, director of medical informatics, are key members of the project. As project director for clinical information systems, Kahn is responsible for integrating patient information from all of the BJC hospitals. As the University's project director for imaging and communications initiatives, Blaine oversees the development of efficient, cost-effective ways to transmit diagnostic radiology images as well as images from other medical specialties across Spectrum's wide-reaching electronic network.

As the **FIRST INTEGRATED HEALTH INFORMATION SYSTEM** nationwide to link an academic medical center with suburban and rural health facilities, Project Spectrum is capable of supporting both video and high-resolution image transmission to more than 5,000 affiliated physicians in a 250-mile radius. The system is scheduled for enterprise-wide operation in late 1997. **MIR**



FISH



SALAMANDER



CHICK



HUMAN



Ontogeny Recapitulates Phylogeny



**T**o many of us "mitosis" may sound like a foreign language. To **MICHAEL MACKEY**, a PhD cancer biologist, this term is a familiar steppingstone in his search for an effective method of treating cancer with an age-old therapy, hyperthermia.

The process that cells undergo to achieve normal cell division is called mitosis: After a cell divides, its DNA must be doubled before the cell can divide again. Premature or abnormal mitotic events lead to cell death. **HYPERTHERMIA** uses high temperatures to trick cells into dividing or attempting to divide before the completion of normal mitosis. Based on results from numerous rodent studies and on the assumption that temperature levels causing rodent cell death elicited the same result in human cells, researchers and clinicians nationwide followed the principle that hyperthermia was not effective with temperatures lower than 43° Celsius. But those same high temperatures that kill cancer cells often are not tolerated well by patients and cause technical difficulties with the heat delivery systems.

In studies supported in 1993 by a National Institutes of Health grant, Mackey discovered that unlike rodent cells, human cell death continues at temperatures as low as 41.5°C. Further research, aided by computer and mathematical modeling, yielded important information that challenges accepted hypotheses about the biochemical basis for premature cell division. For example, conventional theory holds that premature cell division is caused by events occurring during the regulated **MITOTIC PROCESS**. Mackey proposes there are "cascades of molecular events" and if any one of the components of the cascades are present in abnormally high amounts, the cells can be tricked into dividing before DNA replication is completed. He and Dr. Paul Swanson, a Washington University surgical pathologist, are examining cells by electron microscopy to identify new modes of cell killing.

Mackey's original research has numerous spinoffs that all impact on the ultimate goal of clinical hyperthermia: Control the cell growth and stop the tumor from growing. One aspect (which Mackey calls "Ontogeny Recapitulates Phylogeny") focuses on a biological notion that embryonic cells from different organisms are very similar during early development, with each species taking a shared path on its way to adulthood and developing a series of steady states. Another spinoff involves the identification of distinguishable differences between live organisms and dead organisms by comparing the rates of specific biochemical processes. One theory states that cells maintain a homeostatic or steady state even though they are constantly bombarded by external and internal influences, but another, the dynamic systems theory (also called chaos), purports that some aspects of biological systems are random or chaotic. Using a computer model, Mackey unified the two concepts and discovered the rates, although chaotic, actually mirrored each other, resulting in an overall steady state.

Controlling cell growth is a complex problem at the molecular level, but developing models as Mackey has allows cancer biologists to fine-tune experimentation and to develop hypotheses that can be tested. Lowering the temperature rate used for hyperthermia is showing good results in the treatment of deep-seated tumors and holds promise for a number of site-specific tumors such as lung, prostate, and brain. **MIR**







*Since the first MIR diagnostic radiology residents arrived in 1931, more than 800 of the world's brightest young physicians have received their radiology, nuclear medicine, and radiation oncology training at the Institute. The affiliation between Washington University School of Medicine and the BJC hospital network provides for a wellspring of cases from which the*

**RESIDENTS AND FELLOWS,** *as well as medical students and technologists, can learn more about the detection and healing of diseases. The Institute's teaching programs are important pathways for administering quality patient care.*

The four-year diagnostic residency program offers instruction and guidance by recognized experts in the disciplines of abdominal radiology and ultrasonography, neuroradiology, nuclear medicine, vascular and interventional radiology, magnetic resonance imaging, chest radiology, computed tomography, musculoskeletal and emergency radiology, breast imaging, and pediatric radiology. A specialized five-year program to prepare the clinician scientist for an academic radiology career combines general diagnostic radiology training, full-time research opportunities, and concentrated instruction in a radiology subspecialty. As a result of the 1994 merger of the diagnostic residency programs at Barnes and Jewish hospitals, MIR's 68-member training program is the **LARGEST OF ITS KIND** in the United States.

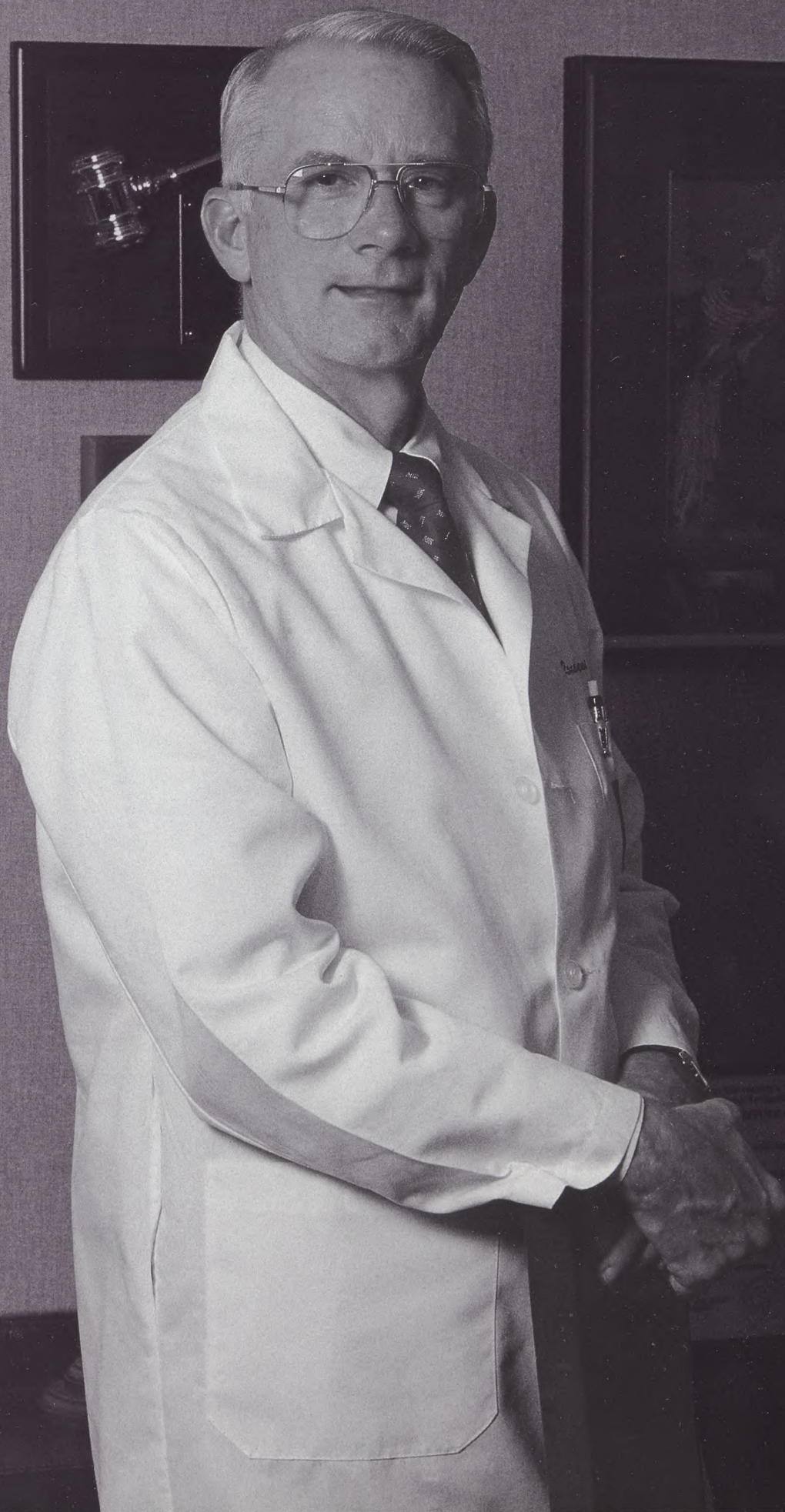
MIR's nuclear medicine/nuclear radiology residency program has a strong heritage — five decades of Washington University experience in the application of radionuclide tracers to the biomedical sciences. Two approved learning experiences are available: A two-year program, open to physicians with at least one but preferably two or more years of postgraduate training in another specialty, fulfills the training requirements for American Board of Nuclear Medicine (ABNM) certification. The one-year option for applicants who have completed a diagnostic radiology residency meets the requirements for certification in diagnostic radiology with special competence in nuclear radiology (and usually allows the trainee also to be certified by the ABNM).

The radiation oncology and medical physics residency programs combine **RESEARCH** and **CLINICAL EXPERIENCES** to strengthen and support the fight against cancer. Accredited in 1971, the radiation oncology program is available to applicants who have completed an internship and provides a four-year exposure to a multidisciplinary approach to the treatment of cancer. During a six-month research rotation, residents participate in a biology or physics project that is supervised by a staff member. In the two-year medical physics program, trainees gain experience in solving fundamental problems in dosimetry, hyperthermia, and three-dimensional treatment planning.

Graduates of MIR's training programs practice in 48 states and in 25 foreign countries. As further testimony to Mallinckrodt Institute's reputation as a leader in education, more than 50 current chairs of academic radiology departments worldwide received their training or taught at the Institute. **MIR**

At left, Daniel Keleti, MD, 1994-1995  
chief resident, Radiation Oncology  
Center.







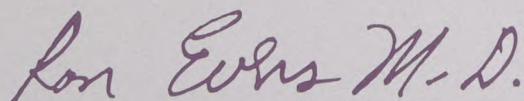
**T**he past academic year was one of accomplishments, strategic planning, and major investments in the academic and clinical futures of Mallinckrodt Institute of Radiology at Washington University. We live in and must respond to several environments that are all changing rapidly: Washington University, the specialty of radiology, and the United States health care system. At Mallinckrodt Institute, we have made major commitments to the traditional academic medical responsibilities of **PATIENT CARE, EDUCATION, AND RESEARCH.**

Nationwide, many health care providers are preparing for the onset of managed care and managed competition by combining services to form health care networks. Mallinckrodt Institute is playing an important role in the BJC Health System, Missouri's first health care network, by providing the highest quality diagnostic and therapeutic patient care possible.

MIR's diagnostic and radiation oncology residency programs continue to attract the top radiology candidates in the nation, as is evidenced by the exceptional results of the yearly Matching Program. We are dedicated to preserving the integrity and quality of the Institute's residency and fellowship programs while broadening our research graduate student program.

The Mallinckrodt Institute of Radiology at Washington University Imaging Center is the first step in MIR's major expansion of imaging sciences research. The **IMAGING CENTER**, which opened last November, provides a centralized location for studies focusing on positron emission tomography, magnetic resonance imaging, electronic radiology and computer science, neuroimaging, and radiopharmaceutical development. The growth in our research programs will emphasize collaborations with other Washington University departments.

The past academic year has been a time of growth for the Institute. We have expanded not only in size (60,000 square feet of new or remodeled research space) but in strength (138 faculty, 90 of whom are tenured or on tenure track). Through careful planning and the effective use of our important resources, the Institute can become the highest rated academic radiology department in the United States. At MIR we are not just responding to an uncertain world, we are creating changes that will improve our scholarly activities and consequently provide **BETTER SERVICE TO OUR PATIENTS.**



Ronald G. Evens, MD  
Director of the Institute



## 1994-1995 FULL-TIME FACULTY OF THE MALLINCKRODT INSTITUTE OF RADIOLOGY

Carolyn J. Anderson, PhD	Louis A. Gilula, MD	James D. Matthews, MD	Henry D. Royal, MD
D. Claire Anderson, MD	Harvey S. Glazer, MD	John W. Matthews, DSc	Stuart S. Sagel, MD
Carlos F. Aquino- Aponte, MD	Prabhat C. Goswami, PhD	William H. McAlister, MD	Kondapuram S. Sampathkumaran, MS
Dennis M. Balfe, MD	Mary V. Graham, MD	Timothy J. McCarthy, PhD	David J. Scherer, MS
Mark M. Bahn, MD, PhD	Perry W. Grigsby, MD	Bruce L. McClennan, MD	Alan E. Schlesinger, MD
Gulab Bhatia, MS	Robert J. Gropler, MD	Kevin W. McEnery, MD	Sally W. Schwarz, MS
Premisri Barton, MD	Fernando R. Gutierrez, MD	Elizabeth Gerard McFarland, MD	Janice W. Semenkovich, MD
Harold F. Bennett, MD	E. Mark Haacke, PhD	Robert C. McKnight, MD	Gary D. Shackelford, MD
G. James Blaine, DSc	William B. Harms, BS	William B. Mehard, MD	Vijay Sharma, PhD
Joseph A. Borrello, MD	Jay P. Heiken, MD	Jeff M. Michalski, MD	Peter E. Shile, MD
James A. Brink, MD	Thomas E. Herman, MD	Mary A. Middleton, MD	Barry A. Siegel, MD
Jeffrey J. Brown, MD	Marshall E. Hicks, MD	William D. Middleton, MD	Cary L. Siegel, MD
Kun San Chao, MD	Ryuji Higashikubo, PhD	Tom R. Miller, MD, PhD	Marilyn J. Siegel, MD
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DeWitte T. Cross, MD	Fred J. Hodges, MD	Stephen M. Moore, MS	Emily L. Smith, MD
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P. Duffy Cutler, PhD	Paul S. Hsieh, MD	Eduardo G. Moros, PhD	William Straube, MS
Michael D. Darcy, MD	Clayton R. Hunt, PhD	Daniel F. Mullen, DDS	Marie E. Taylor, MD
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Carmen S. Dence, MS	Eric E. Klein, MS	Gilbert H. Nussbaum, PhD	William G. Totty, MD
Jeffrey A. Dobkin, MD	Lawrence M. Kotner, MD	Carlos A. Perez, MD	Michael W. Vannier, MD
Steven Don, MD	Andrei Laszlo, PhD	Daniel D. Picus, MD	Thomas M. Vesely, MD
Robert E. Drzymala, PhD	Benjamin C. P. Lee, MD	Thomas K. Pilgram, PhD	Jerold W. Wallis, MD
James R. Duncan, MD, PhD	Henry K. Lee, MD	David Piwnica-Worms, MD, PhD	Ge Wang, PhD
John O. Eichling, PhD	Robert G. Levitt, MD	Linda King Proctor, MD	Todd H. Wasserman, MD
Bahman Emami, MD	Debiao Li, PhD	James A. Purdy, PhD	Michael J. Welch, PhD
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Keith C. Fischer, MD	Weili Lin, PhD	Vallabhaneni V. Rao, PhD	Jeffrey F. Williamson, PhD
Glenn Fletcher, PhD	Daniel A. Low, PhD	William R. Reinus, MD	Franz J. Wippold, MD
Seymour Fox, PhD	Michael A. Mackey, PhD	Tracy L. Roberts, MD	Darryl A. Zuckerman, MD
Mokhtar H. Gado, MD	Robert Malyapa, MD, PhD	Douglas D. Robertson, MD, PhD	
Russell L. Gerber, MS		Joseph L. Roti Roti, PhD	
David S. Gierada, MD			





Steven Winn, MD, (back to camera) recently combined his radiology skills with his previous veterinarian experience to diagnose an unusual patient — Betsy, a valuable black rhino in the Saint Louis Zoo's breeding program for endangered species. An ultrasound examination revealed an infection in Betsy's reproductive system.



While the Zoo's modern animal hospital has conventional X ray capabilities, Zoo veterinarian Eric Miller (right) calls upon MIR radiologists to assist in diagnosing specific problems requiring other imaging modalities. The long-standing collaboration between the Zoo and Mallinckrodt Institute plays an important role in maintaining the continuity of certain species for future generations.